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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,920	04/20/2007	Lin Zhi	119378-00314 / 1110US	3750

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EXAMINER	
THOMAS, TIMOTHY P	
ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,920	ZHI ET AL.	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35,37-52,54-84,86-136 and 138* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-10,12-18,25-28,30-35,46,99,107,108,120,126,128-131 and 138* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/16/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

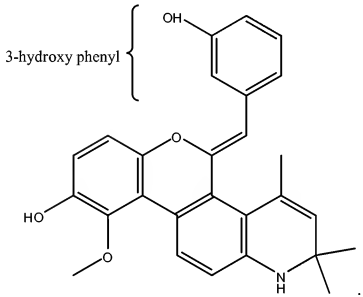
Continuation of Disposition of Claims: Claims withdrawn from consideration are 5,11,19-24,29,37-45,47-52,54-84,86-98,100-106,109-119,121-125,127 and 132-136.

DETAILED ACTION

Election/Restrictions

1. Claim 35 is rejoined for examination, because it reads on the originally elected compound.

2. The compounds under examination are expanded to include the 3-hydroxy phenyl compound specie:



This is a compound with the core structure of Formula I, where R_1 is Formula II and R_3 is OR_{16}, and R_2, R_4-R_6 and R_{16} are each H. This would be compound 109 of claims 107-108 (pp. 28, 44 of claims).

3. This application contains claims 5, 11,19-24, 29, 37-45, 47-52, 54-84, 86-98, 100-106, 109-119,121-125,127 and 132-136 drawn to an invention nonelected with traverse in the reply filed on 6/3/2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Response to Arguments

4. Applicants' arguments, filed 2/25/2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

5. Applicant's arguments with respect to rejoinder of claims have been fully considered but they are only persuasive in part.

Applicant argues the Office Action states that claim 35 does not read on the elected species; that claim 35 recites that R_6 is fluoro, because the substituent is freely rotatable about its axis of connection, when rotated 180°, the fluoro group would occupy the position of substituents R_2. This argument is persuasive; the withdrawal of claim 35 was an inadvertent omission, in part based on applicant's reply to the specie election filed 6/3/2008, which did not identify claim 35 as reading on the elected compound. Therefore, claim 35 is rejoined for examination.

Applicant further argues that claim 128 was designated as not reading on the elected species. It is not clear what is meant by this argument; claim 128 was not withdrawn in Items 3-4 on p. 3 of the Office Action, nor designated as withdrawn on the PTOL-326 form; the claim was included in four separate rejections, which are even so identified in applicant's reply filed 2/25/2009, on p. 65, 67 and 69, and designated as rejected on the PTOL-326 form.

6. Applicant's arguments, see pp. 64-65, filed 2/25/2009, with respect to the declaration have been fully considered and are persuasive. The objection to the Declaration has been withdrawn.

7. Applicant's arguments, see pp. 65-66, filed 2/25/2009, with respect to the rejection under 35 USC 112, 2nd paragraph have been fully considered and are persuasive. The rejection of claims 1-4, 6-10, 12-18, 25-28, 30-34, 36, 46, 120, 126, 128, 130, 131 and 138 has been withdrawn.

8. Applicant's arguments, see p. 67, filed 2/25/2009, with respect to the rejection(s) of claim(s) 1-4, 6-10, 12-18, 25-28, 30-34, 36, 46, 120, 126, 128, 130, 131 and 138 under 35 USC 112, 1st paragraph have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the claim amendment, as presented below.

9. Applicant's arguments, see pp. 67-69, filed 2/25/2009, with respect to the rejection(s) of claim(s) 1-4, 6-10, 12-18, 25-28, 30-34, 36, 46, 120, 126, 128, 130, 131 and 138 under 35 USC 102 have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made as presented below.

The rejection is withdrawn based on the claim amendment removing "derivatives" for which the identified compound read on the claims. The alternate rejection, presented below, is necessitated by this claim amendment.

10. Applicant's arguments, see pp. 69-76, filed 2/25/2009, with respect to the rejection under 35 USC 103 have been fully considered and are persuasive. The rejection of claims 1-4, 6-10, 12-18, 25-28, 30-34, 36, 46, 99, 107-108, 120, 126, 128, 130, 131 and 138 has been withdrawn.

The prior art rejection is withdrawn due to the unexpected larger ratio of GR/PR selectivity of the 2-fluoro, 3-methyl phenyl compound over the prior art 2,3-difluoro phenyl compound, as demonstrated by the Lin Zhi Declaration filed 2/25/2009, p. 5.

Claim Objections

11. Claims 35 and 128 are objected to because of the following informalities: claim 35 states "does not read on species" after the period; claim 128 states, "we said it read on the species" after the period. These phrases appear to be applicant's working notations and have no meaning in the claims. Additionally, a claim is to be a single sentence that ends with a period; in each of these claims there is language after the period. Appropriate correction is required.

Claim Rejections - 35 USC § 112

12. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

13. Claims 1-4, 6-10, 12-18, 25-28, 30-35, 46, 99, 120, 126, 128, 130 and 138 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is necessitated by the claim amendment to claim 1 adding an ester, enol ether, enol ester, solvate or hydrate of a compound of Formula 1.

Claim 1 recites a pharmaceutically acceptable ester, enol ether, enol ester, solvate or hydrate of a compound of Formula 1. While salts do have written description, none of the other genus terms has sufficient written description to demonstrate that applicant was in possession at the time of filing of esters, enol ethers, enol esters, solvates and hydrates of the elected compound. A review of the specification did not identify structures of esters, enol ethers, enol esters; what attachment site(s) on the elected compound are contemplated, which ester or ether moieties would be used, nor is there description of how to make such compounds. Furthermore, no solvate or hydrate of the elected compound is described.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a compound of Formula I or a pharmaceutically acceptable salt, ester, enol ether, enol ester, solvate or hydrate thereof.

(1) Level of skill and knowledge in the art:

The level of skill and knowledge in the art are high.

(2) Partial structure:

Formula I has been disclosed, along with a number of compounds, which include the elected compound. However, no ester or ether moieties have been disclosed, nor which solvents would be used in making a solvent.

(3) Physical and/or chemical properties and (4) Functional characteristics:

The disclosed compounds bind to glucocoricoid receptors and/or modulate the activity of glucocorticoid recptors. Esters would somewhere in the molecule contain an ester moity; ethers would contain an ether moiety. Solvents would contain a small whole number ratio of solvent:compound molecules; hydrates would contain a small whole number ratio of water:compound molecules.

(5) Method of making the claimed invention:

No method or making any ester, enol ether, enol ester, solvate or hydrate of the elected compound have been disclosed.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1-4, 6-10, 12-18, 25-28, 30-35, 46, 99, 120, 126, 128, 130 and 138 is/are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are limitless to any ester, enol ether, enol ester, solvate or hydrate or of the elected compound, or of any compound of Formula I. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of the elected compound and compounds identified in the specification tables and/or

examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 103

14. Claims 1-4, 6-10, 12-18, 25-28, 30-34, 99, 107-108, 120, 126, 128, and 130 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coghlan et al. (WO 02/02565 A2; 2002; IDS reference BA) and Patani et al. ("Bioisosterism: A Rational Approach in Drug Design"; 1996; Chem. Rev.; 96:3147-3176; cited in a prior Office Action).

This rejection is necessitated by the claim amendment removing "derivatives" of formula I, on which the previous rejection under 35 USC 102 was based.

Coghlan teaches a compound with the same core structure of Formula I, where R_1 is Formula II and R_3 is F, and R_2 and R_4-R_6 are each H (3-fluoro analog of the elected compound; p. 231, Example 374); compounds are useful as glucocortiocoid-

selective anti-inflammatory agents (title); pharmaceutical compositions that comprise a compound and a pharmaceutically acceptable carrier (p. 59, lines 1-3). Coghlan does not teach the 3-hydroxy phenyl compound under examination. Patani teaches bioisosteres that elicit similar biological activity, due to common physicochemical properties of the bioisosteres (p. 3148, 2nd paragraph; bioisosteric replacements include hydroxy group for fluoro (p. 3152, Figure 11; p. 3148, Table 2). It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the 3-fluoro compound of Coghlan Example 374 by substituting a -OH group for the F at the 3 phenyl position, which would have given the 3-OH phenyl compound (coumpound 109 of claims 107-108). The motivation to modify the compound would have been the similar activity expected for the bioisosteric substitution of hydroxy group for the fluoro atom, as taught by Patani. Absent evidence to the contrary, the properties recited in claims 126, 128 and 130 would be expected based on the teaching of Coghlan, and would be characteristic properties of a compound of the claims.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe inherently includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Conclusion

15. No claim is allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
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